ORIGINAL ARTICLE

Occupational exposure in dentistry and miscarriage

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Background: Information on the reproductive effects of chemical exposures in dental work is sparse or inconsistent.
Aim: To investigate whether dental workers exposed to acrylate compounds, mercury amalgam, solvents or disinfectants are at an increased risk of miscarriage.
Methods: The study was conducted among women dental workers and a comparison group of workers occupationally unexposed to dental restorative materials. Information on pregnancies was obtained from national registers and outpatient units of hospitals. Data on occupational exposure were obtained using postal questionnaires. The final study population included 222 cases of miscarriage and 498 controls (births). An occupational hygienist assessed exposure to acrylate compounds, disinfectants and solvents. Exposure to other agents was assessed on the basis of the questionnaire data. Odds ratios (ORs) and confidence intervals (CIs) were estimated using conditional logistic regression.
Results: The ORs adjusted for confounding factors were increased for moderate-exposure and high-exposure categories of mercury amalgam (OR 2.0, 95% CI 1.0 to 4.1 and OR 1.3, 95% CI 0.6 to 2.5, respectively). The risk was slightly increased for the highest-exposure category of 2-hydroxyethylmethacrylate (OR 1.4, 95% CI 0.7 to 2.6) and polymethylmethacrylate dust (OR 1.4, 95% CI 0.8 to 2.4). A slightly increased risk was also detected for likely exposure to organic solvents (OR 1.4, 95% CI 0.8 to 2.3) and disinfectants (OR 1.5, 95% CI 0.9 to 2.7).
Conclusions: No strong association or consistent dose–response relationship was observed between exposure to chemical agents in dental work and the risk of miscarriage. A slightly increased risk was found for exposure to mercury amalgam, some acrylate compounds, solvents and disinfectants. These findings indicate that the possibility of a weak association between exposure to these agents and an increased risk of miscarriage cannot be excluded.

Dentists and dental nurses/hygienists may be exposed to several potential reproductive health hazards. These include mercury, acrylate compounds, organic solvents, disinfectants, anaesthetic gases and *x* radiation. Exposure to mercury and acrylate compounds occurs during the placement of amalgam or composite fillings, the finishing and polishing of fillings, and the removal of old fillings. The use of amalgam in dentistry has, however, decreased during the past decade, whereas the use of composites consisting of methacrylic compounds has increased. In Finland, composite resin was the most common material used for restorations in 1997.[1] In dental laboratories, workers are also exposed to acrylate compounds (methyl methacrylate (MMA)), as well as to metal dusts and fumes.

Data on the effects of acrylate compounds on reproductive health are sparse and conflicting. In two animal studies, inhalation exposure to MMA induced early fetal deaths and haematomas.[2 3] However, in two other studies, no signs of embryo or fetal toxicity were observed in exposed animals.[4 5] Intraperitoneal injection of several types of methacrylate esters into pregnant rats resulted in resorption, fetal death or decreased fetal size.[6] In addition, some dental materials (Vitrebond and AH26) have elicited genotoxic responses in test systems,[7] and a compound commonly used in restorative materials (bisphenol A diglycidylmethacrylate) has induced embryotoxic effects in the mouse embryonic stem cell test.[8] Intragastric administration of leached components from a resin-based dental composite has induced adverse effects on fertility and on the reproductive system of female mice.[9]

Results of human studies on acrylate compounds are inconsistent. Fedotova[10] found an increased risk of miscarriage among industrial workers exposed to MMA. Malformations, hypoxia and prematurity were also observed in the children of the exposed women. On the other hand, exposure to acrylate compounds during the placement of tooth-coloured restorations was not related to decreased fertility among dentists in a Norwegian study.[11]

Toxicological studies suggest that mercury may have detrimental effects on health. Higher urinary mercury concentrations have been measured in dentists who make amalgam restorations than in dentists not using amalgam,[12] or in an occupationally unexposed reference group.[13] In addition, it has been shown that inorganic mercury accumulates in the placenta and that a substantial fraction of maternal blood mercury reaches the fetus.[14] The results of epidemiological studies on the effects of mercury on dental workers' reproductive health have been conflicting.[11 15–21]

In addition to restorative materials, dental personnel may be exposed to organic solvents and active (antibacterial) ingredients of disinfectants when they clean surfaces with solvent-based disinfectants or instruments with water-based agents. Previously, high exposure to solvents has been associated with an increased risk of miscarriage in various occupational groups.[22] Examples of active ingredients of the disinfectants used in dental care are o-phenylphenol, benzoyl-p-chlorophenol and n-alkyl-n-benzyl-n,n-dimethylammonium chloride. Their reproductive effects have not been studied in humans.[23 24] The results of animal experiments on o-phenylphenol have been contradictory; however, some adverse effects were found at high doses.

Abbreviations: HEMA, 2-hydroxyethylmethacrylate; MMA, methyl methacrylate; PMMA, polymethylmethacrylate; TEGDMA, triethyleneglycol dimethacrylate

The aim of our study was to investigate whether workers occupationally exposed to acrylate compounds, mercury, solvents and disinfectants, as well as ionising radiation, are at an increased risk of miscarriage.

MATERIALS AND METHODS

The source population of the study was composed of women belonging to the national trade unions of dentists, dental nurses and hygienists, dental technicians and dental laboratory workers, as well as pharmacists, secretaries and receptionists in health care. The pharmacists, secretaries and receptionists in health care represented women working in the health care sector but occupationally unexposed to acrylate compounds and mercury. The trade unions were asked to provide information on women who were born in 1951 or later, and who had belonged to the union during 1992–9. A total of 12 992 women were identified. The study was approved by the Ethics Committee for Research in Occupational Health and Safety.

Information on births in the years 1992–8 was obtained from the Finnish Medical Birth Register, and the data on miscarriages came from the Hospital Care Register of the National Research and Development Centre for Welfare and Health (Helsinki, Finland). Altogether, 8537 births, 1002 miscarriages and 801 other pregnancies (induced abortion or extrauterine pregnancy) of the union members were identified. In addition, information was collected nationally from the hospitals on patients with miscarriage who were treated in the outpatient units of the hospitals and not included in the Hospital Care Register. Altogether, 227 miscarriages were found. The coverage of the Medical Birth Register is considered complete, and the quality of its data has been found to be high for most of the variables.[25 26] We have previously estimated that 80–90% of all recognised miscarriages can be detected from the Hospital Care Register and local registers of the outpatient departments of the hospitals.[27]

A pregnancy was eligible for study if it had started between 1992 and 1998, if the woman was a member of the union during the first 3 months of pregnancy and if she was aged 25–39 years at the beginning of the pregnancy. The first eligible pregnancy of a woman during the study period was selected for study.

The study used a case–control approach. The cases were women whose pregnancy under study was a miscarriage, and the controls were selected from pregnancies that had ended in a delivery. For ethical reasons, the births of seriously malformed children were excluded from the potential controls with the help of data obtained from the Finnish Register of Congenital Malformations. The frequency of induced abortion was small (4.3%) in the study population, and the differences in the frequencies between the occupational groups were also small. The frequency was highest among the secretaries and receptionists (5.7%) and lowest among the dentists (3.1%).

The cases and controls were frequency matched for age in the following four categories: 25–28, 29–32, 33–36 and 37–39 years. In the age strata, the controls were randomly selected, and the sampling fraction for the potentially exposed and unexposed pregnancies was the same. Altogether, 358 cases and 716 controls (twice the number of cases) were identified.

Data on occupation, working tasks and occupational exposure during the first trimester of pregnancy were obtained using postal questionnaires. The questionnaire for the dentists and dental nurses/hygienists included questions on the frequency of placing and removing amalgam and composite resin fillings and the trade names of the used products, the frequency of using disinfectants and nitrous oxide, and the frequency of staying in the same room with the patient during the *x* radiation. The dental technicians and dental laboratory workers were asked about the number of hours involved in tasks with exposure to MMA, and the use of local exhaust ventilation and protective devices. The pharmacists were asked about the frequency of handling drugs that are potentially harmful to pregnancy and were not handled in closed/sealed packages. All the participants were asked about their use of solvents (solvent-based cleaning agents). Information on the workers' medical condition, reproductive history, length of gestation, number of amalgam fillings, smoking and use of alcohol was also requested. Furthermore, data on the fathers' working tasks and exposure to some occupational and lifestyle factors during the 3 months before the conception of the study pregnancy were sought. These data were collected 3–9 years after the pregnancies.

After three postings the response rate was 68% (66% for the cases and 70% for the controls). The response rate varied slightly by occupation. It was highest for the pharmacists (75%) and lowest for the dental nurses and hygienists (64%; table 1). The most distinct difference in the response rate between the cases and controls occurred for the dental technicians and laboratory workers. The study pregnancy was confirmed by 94.5% of the case respondents and by 99.6% of the control respondents. There were 15 women who did not confirm the study pregnancy in the questionnaire; they were excluded (2 births, 13 miscarriages). The final analysis was limited to the confirmed pregnancies, including 222 cases and 498 controls.

Assessment of exposure

An occupational hygienist assessed the participants' exposure to acrylate compounds (2-hydroxyethylmethacrylate (HEMA), methyl methacrylate (MMA) and polymethylmethacrylate (PMMA) dust), disinfectants and solvents. The assessment was conducted blinded to the participant's case–control status. The assessment was made on the basis of the questionnaire information, earlier industrial hygiene measurements at Finnish dental offices and dental laboratories,[28–30] and data from previous studies of exposure conditions.[31] Exposure to mercury amalgam, triethyleneglycol dimethacrylate (TEGDMA), anaesthetic gases and ionising radiation was assessed on the basis of the questionnaire data only.

Exposure to HEMA was assessed by the frequency of restoration cementation, and replacement of composite resin

Table 1 Response rate of the cases and controls by occupation

Occupation	Cases n (%)	Controls n (%)	Total n (%)
Dental technicians and laboratory workers	6 (54.6)	20 (76.9)	26 (70.3)
Dentists	49 (67.1)	106 (68.0)	155 (67.7)
Dental nurses and hygienists	86 (61.4)	183 (65.4)	269 (64.1)
Pharmacists	69 (74.2)	139 (76.0)	208 (75.4)
Receptionists and departmental secretaries in health care	25 (61.0)	52 (73.2)	77 (68.8)
Total	235 (65.6)	500 (69.8)	735 (68.4)

Table 2 Odds ratios for miscarriage as regards potential risk factors*

Factor	Cases	Controls	OR	95% CI
Pregnancy history				
Previous miscarriage	38	66	1.4	0.9 to 2.2
Previous induced abortion or extrauterine pregnancy	19	25	1.8	1.0 to 3.4
Previous births				
1	61	135	1.0	0.7 to 1.4
2	41	110	0.8	0.5 to 1.3
⩾3	13	26	1.1	0.5 to 2.4
Use of intrauterine device or pills at conception	6	9	1.6	0.6 to 4.5
Diseases and drugs				
Cervicitis	9	28	0.7	0.3 to 1.6
Inflammation of uterine cavity	7	4	4.0	1.1 to 13.6
Oophoritis	6	11	1.3	0.5 to 3.5
Other disease of genital organs†	4	3	3.1	0.7 to 14.0
Medical examination because of infertility	16	24	1.5	0.8 to 3.0
Diabetes (treated with insulin)	3	4	1.7	0.4 to 7.7
Disease of the thyroid gland	4	9	1.0	0.3 to 3.3
Fever	25	60	0.9	0.5 to 1.5
Potentially harmful drugs‡	5	8	1.4	0.5 to 4.3
Other maternal factors				
Number of own amalgam fillings				
5–9	105	219	1.1	0.7 to 1.7
⩾10	69	168	1.0	0.6 to 1.6
Smoking				
1–4 cigarettes/day	7	19	0.9	0.4 to 2.1
⩾5 cigarettes/day	8	9	2.1	0.8 to 5.4
Alcohol consumption				
<1 drink a week	44	129	0.7	0.5 to 1.1
⩾1 drinks a week	15	19	1.9	0.9 to 3.8
BMI (reference group 20–25; kg/m^2)				
<18	5	6	1.7	0.5 to 5.8
18–19	15	54	0.6	0.3 to 1.1
26–27	28	67	0.9	0.6 to 1.5
28–30	16	31	1.1	0.6 to 2.1
>30	17	39	0.9	0.5 to 1.7
Paternal factors				
Smoking				
1–4 cigarettes a day	12	25	1.1	0.5 to 2.2
5–14 cigarettes a day	22	53	0.9	0.6 to 1.6
⩾15 cigarettes a day	25	54	1.1	0.6 to 1.8
Alcohol consumption				
<2 drinks a week	67	167	0.9	0.5 to 1.5
2–6 drinks a week	84	192	1.0	0.6 to 1.6
7–14 drinks a week	37	75	1.1	0.6 to 2.0
Occupational exposure				
Solvents	76	182	1.0	0.7 to 1.3
Metal fumes and dusts	61	127	1.2	0.8 to 1.7
Welding fumes or soldering smoke	49	105	1.1	0.7 to 1.6
Pesticides	14	22	1.5	0.7 to 3.0
Temperatures of >30°C at work	42	100	0.9	0.6 to 1.4

BMI, body mass index.
*The models include a category for missing information when necessary.
†Other genital diseases: polycystic ovary syndrome, myoma, endometrial polyp, actinomycosis and adenomyosis.
‡Drugs potentially harmful to pregnancy: anticonvulsants, tetracyclines, and anti-inflammatory analgesics (excluding paracetamol).

restorations or glass ionomer restorations (if a product including HEMA was used). Exposure to MMA was defined as low (air concentration <1 ppm) for all dentists and dental nurses/hygienists, as well as for all dental technicians and laboratory workers who handled the raw materials of acrylic resins/plastics or worked in the room where they were handled for not more than 2 h a week. Dental technicians and dental laboratory workers who worked for >2 h/week with these materials belonged to the high category (1–20 ppm).

All the women who used protective equipment when grinding acrylate products or who worked in the same room for <7 h/week, as well as all those who worked in dental offices, were classified as exposed to organic PMMA dust. The concentration of PMMA in their working air was assessed as <0.5 mg/m^3. Only three women were defined as exposed to higher concentrations (0.5–1.5 mg/m^3), and therefore only one exposure category was formed. Exposure to TEGDMA was determined by the number of removed composite resin restorations per week, because it has been found that TEGDMA is released into the air mainly during the removal of old composite resin restorations.[29]

Exposure to mercury amalgam was classified by the number of amalgam fillings made and removed per week. Cumulative exposure to mercury amalgam was assessed by years of exposure before pregnancy. If a woman stayed in the same room with the patient during *x* radiation, she was considered

Table 3 Crude and adjusted* odds ratios for miscarriage as regards occupational exposure to acrylate compounds and mercury amalgam; six multivariate models

Exposure	Level of exposure	Cases	Controls	OR Crude	OR Adjusted	95% CI
HEMA	Not exposed	116	265	1.0	1.0	Ref.
	<10 times a week	11	22	1.2	1.5	0.6 to 3.5
	11–40 times a week	57	121	1.1	1.3	0.7 to 2.3
	>40 times a week	31	70	1.0	1.4	0.7 to 2.6
MMA concentration in air	Not exposed	151	340	1.0	1.0	Ref.
	<1 ppm	63	140	1.0	1.3	0.7 to 2.3
	1–20 ppm	6	13	1.0	1.1	0.4 to 3.2
PMMA dust	Not exposed	125	294	1.0	1.0	Ref.
	Exposed	92	192	1.1	1.4	0.8 to 2.4
TEGDMA	Not exposed	125	287	1.0	1.0	Ref.
	⩽10 times a week	50	111	1.0	1.3	0.7 to 2.4
	>10 times a week	46	98	1.1	1.4	0.8 to 2.6
Mercury amalgam†	Not exposed	120	270	1.0	1.0	Ref.
	Very low	9	23	0.9	1.2	0.5 to 3.0
	Low	39	98	0.9	1.3	0.7 to 2.3
	Intermediate	23	36	1.4	2.0	1.0 to 4.1
	High	28	61	1.0	1.3	0.6 to 2.5
Number of years of using mercury amalgam before pregnancy† (daily or nearly daily)	Not used or stopped ⩾1 year earlier	147	344	1.0	1.0	Ref.
	⩽5 years	19	41	1.0	1.3	0.6 to 2.8
	6–10 years	22	38	1.3	1.7	0.8 to 3.5
	>10 years	25	62	1.0	1.3	0.6 to 2.5

HEMA, 2-hydroxyethylmethacrylate; MMA, methyl methacrylate; PMMA, polymethylmethacrylate; TEGDMA, triethyleneglycol dimethacrylate.
*The models include employment, age, time period, exposure to solvents, *x* radiation, previous miscarriage, induced abortion or extrauterine pregnancy, use of intrauterine device or pills at conception, previous intrauterine inflammation, other previous genital disease, diabetes, previous medical infertility examination, use of potentially harmful drugs, smoking and use of alcohol; the models include a category for missing information on each examined agent.
†The model also includes the number of own amalgam fillings.

exposed to ionising radiation. Exposure to solvents and disinfectants was defined as potential or likely. The trade names of the products were used in the assessment of exposure to ethanol and isopropanol.

Exposure to the disinfectants used for cleaning the instruments was classified as high if the woman cleaned the instruments ⩾6 times a week, or if the task took place in the dentist's workroom and/or the instruments were in an open bowl. If cleaning was done 1–5 times a week in similar conditions, exposure was defined as intermediate. Also, if the cleaning was done ⩾6 times a week, but was done in a different room and the bowl was covered, exposure was classified as intermediate. The exposure of other women working with disinfectants was assessed as low. If a woman was not using disinfectants, the bowl was in a different room and the task was also done in a different room, she was considered unexposed.

Statistical methods

Odds ratios (ORs) and confidence intervals (CIs) were estimated using conditional logistic regression (procedure PHREG, SAS V.8.2). The potential maternal and paternal confounding factors were selected on the basis of prior knowledge and included in the final models on the basis of their association with miscarriage (table 2). Employment was included in all the models. The year of beginning of pregnancy (1992–3, 1994–5, 1996–8) was also included in all the models because exposure to some agents had decreased (mercury amalgam) during the study period while exposure to others had increased (HEMA, solvents). Potential confounding by age in the matching strata was adjusted by adding a centred age variable (ie, the deviation of the mother's age from the mean age of the controls in the mother's matching category) to the conditional logistic model.[32] The number of the participants' own fillings was included in the models on mercury amalgam. Exposure to various acrylate compounds and mercury amalgam was highly correlated. Therefore, only exposure to solvents and *x* radiation was adjusted in the multivariate analyses on other chemical agents.

RESULTS

Table 2 shows the frequencies of the cases and controls and the ORs for miscarriage as regards potential confounding factors. Increased ORs indicating an increased risk were observed for the women who had had a previous miscarriage, induced abortion or extrauterine pregnancy, or who had used an intrauterine device or pill at conception. An increased risk was noted also for the women who had had inflammation of the uterus or some other genital disease before the study pregnancy, a medical examination because of infertility, or diabetes treated with insulin and had used drugs potentially harmful to pregnancy. Smoking, use of alcohol and low body mass index (<18) seemed to be related to miscarriage as well.

The risk of miscarriage among all members of the trade unions of dental workers did not differ from the risk of members belonging to the trade unions of pharmacists and receptionists and secretaries in health care (OR adjusted for employment, age and time period 0.9, 95% CI 0.7 to 1.3). Adjustment for other potential confounding factors (previous miscarriage, induced abortion or extrauterine pregnancy, use of intrauterine device or pills at conception, previous intrauterine inflammation, other previous genital disease, diabetes, previous

Table 4 Crude and adjusted* odds ratios for miscarriage as regards occupational exposure to solvents, disinfectants and ionising radiation; six multivariate models

Exposure	Level of exposure	Cases	Controls	OR Crude	OR Adjusted	95% CI
Solvents	Not exposed	59	137	1.0	1.0	Ref.
	Potential exposure	18	39	1.1	1.2	0.6 to 2.5
	Likely exposure	134	287	1.1	1.4	0.8 to 2.3
Ethanol	Not exposed	75	183	1.0	1.0	Ref.
	Exposed	115	240	1.2	1.4	0.8 to 2.4
Isopropanol	Not exposed	125	277	1.0	1.0	Ref.
	Exposed	54	115	1.0	1.4	0.8 to 2.5
Chloroform	Not exposed	154	348	1.0	1.0	Ref.
	Exposed	63	145	1.0	1.3	0.7 to 2.3
Disinfectants	Not exposed	129	305	1.0	1.0	Ref.
	Potential exposure	28	64	1.1	1.4	0.7 to 2.8
	Low	24	46	1.2	1.5	0.7 to 3.0
	Intermediate	31	55	1.3	1.9	1.0 to 3.7
	High	7	23	0.7	0.9	0.3 to 2.4
x radiation	Not exposed	200	501	1.0	1.0	Ref.
	⩽10 times a week	12	40	0.7	0.7	0.3 to 1.6
	>10 times a week	10	17	1.3	1.6	0.7 to 4.2

*Adjusted for employment, age, time period, exposure to solvents or other solvents, *x* radiation, previous miscarriage, induced abortion or extrauterine pregnancy, use of intrauterine device or pills at conception, previous intrauterine inflammation, other previous genital disease, diabetes, previous medical infertility examination, use of potentially harmful drugs, smoking and use of alcohol; the models include a category for missing information on each examined agent.

medical infertility examination, use of potentially harmful drug, smoking, use of alcohol and exposure to solvents) gave an OR of 0.9 (95% CI 0.6 to 1.3). No increased risks of miscarriage were seen in any of the specific groups of dental workers (dentists, dental nurses, and dental technicians and laboratory workers) as compared with non-dental workers.

Table 3 shows the crude and adjusted ORs of miscarriage for exposure to mercury amalgam and various acrylate compounds. The adjusted OR of miscarriage was 2.0 (95% CI 1.0 to 4.1) for moderate exposure to mercury amalgam, but lower for the high-exposure category (OR 1.3, 95% CI 0.6 to 2.5). Combining the intermediate-exposure and high-exposure categories gave an adjusted OR of 1.5 (95% CI 0.8 to 2.8). When the association was examined by the duration (number of years) of using mercury amalgam, no consistent association was found. The ORs were slightly increased for exposure to all the acrylate compounds (HEMA, MMA, PMMA and TEGDMA), but there was no consistent dose–response relationship.

Exposure to organic solvents was common in the study population; the proportion of exposed women was 86% among the dental personnel, 73% among the pharmacists and 35% among the secretaries and receptionists. For likely exposure to solvents and individual solvents, the adjusted ORs were slightly increased (table 4). For exposure to disinfectants during instrument cleaning, the adjusted OR was 1.5 (95% CI 0.9 to 2.7), but when the association was examined by the level of exposure, an increased risk was seen for potential exposure and for the low and intermediate categories, but not for the highest-exposure category. Combining the intermediate-exposure and high-exposure categories gave an adjusted OR of 1.6 (95% CI 0.8 to 3.0).

The OR for miscarriage was 1.6 (95% CI 0.7 to 4.2) for the women exposed to *x* radiation by staying >10 times a week in the same room with the patient when *x* rays were used. Because of the small number of exposed women, the association was imprecise (table 4). Exposure to anaesthetic gases and antineoplastic agents was also uncommon (2% exposed), the result being the wide CIs of the estimates (crude OR for anaesthetic gases 0.4, 95% CI 0.1 to 1.7 and crude OR for antineoplastic agents 1.3, 95% CI 0.4 to 4.4).

The distributions of the exposed and unexposed miscarriage cases were examined by week of pregnancy. The proportion of miscarriages was systematically higher for the unexposed than for the exposed cases during early pregnancy (<10 weeks). In contrast, during weeks 10–12, the proportion was higher for the exposed than for the unexposed women. In later pregnancy (⩾13 weeks), no essential difference was found between the exposed and unexposed cases. For example, among the women exposed to PMMA, 32% of the miscarriages occurred before the 10th week of pregnancy, 51% at 10–12 weeks and 17% during the 13th week or later. For the unexposed, the percentages were 48%, 34% and 18%, respectively. For those exposed to mercury amalgam at an intermediate or high level, the percentages were 30%, 52% and 17%, respectively, whereas for those unexposed to amalgam the percentages were 51%, 34% and 15%, respectively. A similar difference in the distribution of spontaneous abortion by week of pregnancy was also found between the women exposed to other acrylate compounds, solvents, disinfectants or *x* radiation, and for the women unexposed to these agents.

DISCUSSION

We found slight, non-significant associations between exposure to some acrylate compounds, mercury amalgam, solvents, disinfectants and *x* radiation, and the risk of miscarriage among the dental personnel. There was no clear indication of a dose–response relationship.

The association of acrylate compounds with miscarriage has not been investigated previously. Our findings on these compounds are, however, consistent with the results of a Norwegian study[11] that showed no association between exposure to acrylate compounds and fertility. In that study, exposure to acrylate compounds was defined as the placement of tooth-coloured restorations. Recent industrial hygiene

measurements have shown that the concentrations of acrylate compounds (MMA, HEMA, I-BMA and TEGDMA) are small in dental clinics in Finland.[29] In dental laboratories, the concentration of MMA has been clearly higher.[28 31] In our data, exposure to MMA in dental laboratories was, however, not related to miscarriage, but the size of the highly exposed group was very small.

The risk of miscarriage was slightly increased for all the exposure categories for mercury amalgam, but no pattern of dose–response was found. Most of the other studies on dentists and dental nurses have shown no association between mercury exposure and reproductive disorders.[11 19–21] However, Rowland *et al*[17 18] observed an increased risk of miscarriage among female dental assistants preparing >50 mercury amalgams a week, and decreased fertility among women preparing >30 amalgams a week and having a high number of poor occupational hygiene factors. We had no information about the industrial hygiene factors of the dental offices. Concentrations of inorganic mercury in blood measured by the Finnish Institute of Occupational Health indicate that the level of exposure is low among dentists and dental nurses, however. All of the concentrations measured during 1993–2000 remained below the reference value for the unexposed (25 nmol/l).

A slight excess of miscarriages was found for those who were exposed to solvents. Increased risks of miscarriage have been observed earlier in industrial populations that may be exposed to high levels of solvents, but no or only slightly increased risks have been noted among workers whose level of exposure is usually low.[22] An increased risk of miscarriage has also been observed among laboratory workers exposed to isopropanol or chloroform.[33 34]

Exposure to solvents in dental offices is usually low according to occupational hygiene measurements.[29] Studies of exposure to solvents in pharmacies have not been reported, but the exposure level can be expected to be about the same as in dental offices. Our results do not contradict those of a previous study on dental assistants that showed no association between solvent exposure and miscarriage.[19] A similar result was obtained among pharmacy assistants, although the exposed workers had an increased risk of stillbirth and perinatal death.[35] An increased risk of miscarriage was seen for the low and intermediate categories of exposure to disinfectants, but not for the highest-exposure category, and thus our study found no consistent association between exposure and miscarriage.

Our study has several strengths. The source population for the study included nearly all dental workers, pharmacists and secretaries or receptionists in health care in Finland. We used hospital records for the identification of miscarriages, and only the pregnancies confirmed by the women themselves were included in the final study population. We believe that the potential for selection bias was small because the population studied was relatively homogeneous (ie, all of the participants worked in the health care sector). We were able to control for several risk factors of miscarriage, such as age, reproductive history, diseases and drugs, smoking and use of alcohol, as well as for fathers' exposure to some occupational and lifestyle factors. We also repeated all the analyses on specific agents by ignoring from the models previous miscarriages, induced abortions or extrauterine pregnancy, intrauterine inflammation and other genital disease. The exclusion of these factors had no or negligible effect on the risk estimates.

Among the exposure estimation methods in common use today, expert assessment of exposure is usually considered the best approach.[36] In our study, an experienced occupational hygienist assessed exposure to most of the agents (acrylate compounds, solvents and disinfectants) without information on the participant's case–control status. The assessment relied on the participants' descriptions of their working tasks, the frequency of performing exposure-related working tasks, and the trade names of the products used, as well as on information on earlier industrial hygiene measurements and on the results of previous studies on exposure.

Exposure to other agents was assessed on the basis of questionnaire data. Women with an adverse pregnancy outcome may recall and report their exposure during pregnancy better than women without adverse outcomes. Most of the validity studies, however, have found little evidence for the existence of recall bias in reporting occupational exposure, although some indications have been noted.[37–39] Therefore, the possibility of recall bias cannot be totally ruled out in this study.

Our study was limited by the simultaneous exposure to various acrylate compounds and mercury amalgam. This limitation makes it difficult to determine the independent effect of specific agents. The numbers of cases and controls were small for some exposure categories and agents (eg, high level of exposure to MMA and exposure to ionising radiation, anaesthetic gases and antineoplastic drugs), limiting the ability of the study to detect any associations with these agents.

In addition, some of the early recognised abortions may not have been treated in hospital, and these as well as all very early, unrecognised losses might be missing from the data. If the exposures preferentially caused early pregnancy loss, the reported OR would have underestimated the true risk.[40] An examination of the distribution of the miscarriage cases by length of gestation showed that the proportion of early miscarriages (<10 weeks) was consistently lower among the exposed than among the unexposed cases, whereas, at 10–12 weeks, it was higher among the exposed than among the unexposed. It is possible that some of the pregnancies of the exposed women had ended at a subclinical stage and were therefore missing from our data. However, this finding should be interpreted with caution because information on the length of gestation was obtained from the women themselves and they may not have recalled the length of gestation accurately.

The response rate of the cases was slightly lower (66%) than that of the controls (70%). We compared the response rate of the cases and controls among the dental care workers (usually exposed to mercury amalgam and acrylate compounds) and among women in other unexposed occupations (unexposed to these agents—ie, pharmacists, receptionists and secretaries) to get some idea of the response rate by exposure and outcome. A similar difference between the cases and controls was apparent

Main messages

- There was no strong association or consistent dose–response relationship between exposure to chemical agents in dental work and the risk of miscarriage.
- A slightly increased but non-significant risk was found for exposure to some acrylate compounds, mercury amalgam, solvents and disinfectants.
- The possibility of a slightly increased risk of miscarriage among exposed dental workers cannot be excluded.

Policy implications

- In general, there is no need to restrict work in dental clinics during pregnancy.
- It is, however, important to conform to good occupational hygiene during pregnancy in dental work.

in the response rates of the dental personnel (cases 63%, controls 67%) and the unexposed group (cases 70%, controls 75%) than in the total population. This finding does not suggest notable selective participation. However, a clear difference in the response rate was noted between the cases (55%) and the controls (77%) working as dental technicians or as dental laboratory workers. This discrepancy may have attenuated the association between high exposure to MMA and miscarriages because all of the highly exposed women were in this occupational category. The possible effect of selective participation on the findings of other exposures cannot be totally excluded either.

No strong association or clear dose–response relationship was observed between occupational exposure to chemical agents or restorative materials and the risk of miscarriage among dental personnel. A slight but non-significant increase in risk was found for exposure to some acrylate compounds, mercury amalgam, solvents and disinfectants. Because of simultaneous exposure to different acrylate compounds and mercury amalgam, the increased risk could not be assigned to any of these restorative materials. On the basis of these findings, the possibility of a slightly increased risk of miscarriage among exposed dental workers cannot be excluded.

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REFERENCES

1 **Forss H**, Widström E. From amalgam to composite: selection of restorative materials and restoration longevity in Finland. *Acta Odontol Scand* 2001;**59**:57–62.
2 **Nicholas CA**, Lawrence WH, Autian J. Embryotoxicity and fetotoxicity from maternal inhalation of methyl methacrylate monomer in rats. *Toxicol Appl Pharmacol* 1979;**50**:451–8.
3 **Luo S**, Gang B, Sun S. Study on embryotoxicity and fetotoxicity in rats by maternal inhalation of low level methyl methacrylate. *Toxicol Lett* 1986;**31**:80.
4 **McLaughlin RE**, Reger SI, Barlalow JA, *et al*. Methylmethacrylate: a study of teratogenicity and fetal toxicity of vapor in the mouse. *J Bone Joint Surg Am* 1978;**60**:355–8.
5 **Solomon HM**, McLaughlin JE, Swenson RE, *et al*. Methyl methacrylate: inhalation developmental toxicity study in rats. *Teratology* 1993;**48**:115–25.
6 **Singh AR**, Lawrence WH, Autian J. Embryonic-fetal toxicity and teratogenic effects of a group of methacrylate esters in rats. *J Dent Res* 1972;**51**:1632–8.
7 **Heil J**, Reifferscheid G, Waldmann P, *et al*. Genotoxicity of dental materials. *Mutat Res* 1996;**368**:181–94.
8 **Schwengberg S**, Bohlen H, Kleinsasser N, *et al*. In vitro embryotoxicity assessment with dental restorative materials. *J Dent* 2005;**33**:49–55.
9 **Al-Hiyasat A**, Darmani H, Elbetieha A. Leached components from dental composites and their effects on fertility of female mice. *Eur J Oral Sci* 2004;**112**:267–72.
10 **Fedotova IV**. Occupational contact of women with methylmethacrylate and the negative tendency in the process of child-bearing. (in Russian) *Gig Sanit*, 1997;**4**:19–21.
11 **Dahl JE**, Sundby J, Hensten-Pettersen A, *et al*. Dental workplace exposure and effect on fertility. *Scand J Work Environ Health* 1999;**25**:285–90.
12 **Lehto T**, Alanen P, Rönnemaa T, *et al*. Urinary mercury concentrations in Finnish dentists. *Proc Finn Dent Soc* 1989;**85**:177–85.
13 **Åkesson I**, Schutz A, Attewell R, *et al*. Status of mercury and selenium in dental personnel: impact of amalgam work and own fillings. *Arch Environ Health* 1991;**46**:102–9.
14 **Ask K**, Åkesson A, Berglund M, *et al*. Inorganic mercury and methylmercury in placentas of Swedish women. *Environ Health Perspect* 2002;**110**:523–6.
15 **Nixon G**, Helsby CA, Gordon H, *et al*. Pregnancy outcome in female dentists. *Br Dent J* 1979;**146**:39–42.
16 **Sikorski R**, Juszkiewicz T, Paszkowski T, *et al*. Women in dental surgeries: reproductive hazards in occupational exposure to metallic mercury. *Int Arch Occup Environ Health* 1987;**59**:551–7.
17 **Rowland AS**, Baird DD, Weinberg CR, *et al*. The effect of occupational exposure to mercury vapour on the fertility of female dental assistants. *Occup Environ Med* 1994;**51**:28–34.
18 **Rowland AS**, Baird DD, Shore DL, *et al*. Nitrous oxide and spontaneous abortion in female dental assistants. *Am J Epidemiol* 1995;**141**:531–8.
19 **Heidam LZ**. Spontaneous abortions among dental assistants, factory workers, painters, and gardening workers: a follow up study. *J Epidemiol Community Health* 1984;**38**:149–55.
20 **Brodsky JB**, Cohen EN, Whitcher C, *et al*. Occupational exposure to mercury in dentistry and pregnancy outcome. *J Am Dent Assoc* 1985;**111**:779–80.
21 **Ericson A**, Källén B. Pregnancy outcome in women working as dentists, dental assistants or dental technicians. *Int Arch Occup Environ Med* 1989;**61**:329–33.
22 **Lindbohm M-L**. Effects of parental exposure to solvents on pregnancy outcome. *J Occup Environ Med* 1995;**37**:908–14.
23 O-phenylphenol (REPROTEXT® Document). REPROTEXT® Database (electronic version). Greenwood Village, CO, Thomson Micromedex, http://csi.micromedex.com/Login.asp (accessed 12 Dec 2006).
24 Alkyl dimethylbenzyl ammonium chloride (REPROTEXT® Document). REPROTEXT® Database (electronic version) Greenwood Village, CO: Thomson Micromedex, http://csi.micromedex.com/Login.asp (accessed 12 Dec 2006).
25 **Gissler M**, Teperi J, Hemminki E, *et al*. Data quality after restructuring a national medical registry. *Scand J Soc Med* 1995;**23**:75–80.
26 **Gissler M**, Rasimus A, Ritvanen A, *et al*. *Reproduction and its trends: statistics on pregnancies, childbirths, sterilizations and congenital malformations in Finland*. SVT Health 1996: 2, Helsinki:National Research and Development Centre for Welfare and Health, 1996:1–86.
27 **Lindbohm M-L**, Hemminki K. Nationwide data base on medically diagnosed spontaneous abortions in Finland. *Int J Epidemiol* 1988;**17**:568–73.
28 **Degerth R**, Hagström P. *Hammaslaboratorioiden työhygieeniset olosuhteet* (*Industrial hygienic working conditions in dental laboratories*). Työolosuhteet 34. Helsinki: Työterveyslaitos, 1981:1–41.
29 **Henriks-Eckerman M-L**, Alanko K, Jolanki R, *et al*. Exposure to airborne methacrylates and natural rubber latex allergens in dental clinics. *J Environ Monit* 2001;**3**:302–5.
30 **Henriks-Eckerman M-L**, Alanko K, Jolanki R, *et al*. Metakrylaatit, pesualkoholit ja luonnonkumiallergeenit hammashoitoloiden ilmassa (Methacrylates, alcohols and natural rubber allergens in the air of dental clinics). *Suomen Hammaslääkärilehti* (*Finn Dent J*), 2001;**1–2**:28–31.
31 **Nayebzadeh A**, Dufresne A. Evaluation of exposure to methyl methacrylate among dental laboratory technicians. *Am Ind Hyg Assoc J* 1999;**60**:625–8.
32 **Rothman KJ**, Greenland S. *Modern epidemiology*. Philadelphia, PA: Lippincott-Raven, 1998:422.
33 **Taskinen H**, Kyyrönen P, Hemminki K, *et al*. Laboratory work and pregnancy outcome. *J Occup Med* 1994;**36**:311–19.
34 **Wennborg H**, Bodin L, Vainio H, *et al*. Pregnancy outcome of personnel in Swedish biomedical research laboratories. *Occup Environ Med* 2000;**42**:438–46.
35 **Schaumburg I**, Olsen J. Congenital malformations and death among the offspring of Danish pharmacy assistants. *Am J Ind Med* 1990;**18**:555–64.
36 **Teschke K**, Olshan AF, Daniels JL, *et al*. Occupational exposure assessment in case-control studies: opportunities for improvement. *Occup Environ Med* 2002;**59**:575–94.
37 **Ahlborg GA**. Validity of exposure data obtained by questionnaire. Two examples from occupational reproductive studies. *Scand J Work Environ Health* 1990;**16**:284–8.
38 **Joffe M**. Validity of exposure data derived from a structured questionnaire. *Am J Epidemiol* 1992;**135**:564–70.
39 **Bauer EP**, Romitti PA, Reynolds SJ. Evaluation of reports of periconceptual occupational exposure: maternal-assessed versus industrial hygienist-assessed exposure. *Am J Ind Med* 1999;**36**:573–8.
40 **Selevan SG**, Lemasters KL. The dose-response fallacy in human reproductive studies of toxic exposures. *J Occup Med* 1987;**29**:451–4.